Gemeinsamer Bundesausschuss

Resolution

of the Federal Joint Committee on an Amendment of the Pharmaceuticals Directive (AM-RL)

Annex XII - Benefit Assessment of Medicinal Products with New Active Ingredients according to Section 35a SGB V: Esketamine (Depression, treatment-resistant, in combination with SSRI or SNRI)

of 19 August 2021

At its session on 19 August 2021, the Federal Joint Committee (G-BA) resolved to amend the Pharmaceuticals Directive (AM-RL) in the version dated 18 December 2008 / 22 January 2009 (Federal Gazette, BAnz. No. 49a of 31 March 2009), as last amended on DD. Month YYYY (Federal Gazette, BAnz AT DD.MM.YYYY BX), as follows:

I. Annex XII shall be amended in alphabetical order to include the active ingredient esketamine as follows:

Esketamine

Resolution of: 19 August 2021
Entry into force on: 19 August 2021
BAnz AT DD. MM YYYY Bx

Therapeutic indication (according to the marketing authorisation of 18 December 2019):

Spravato, in combination with a SSRI or SNRI, is indicated for adults with treatment-resistant Major Depressive Disorder, who have not responded to at least two different treatments with antidepressants in the current moderate to severe depressive episode.

Therapeutic indication of the resolution (resolution of 19 August 2021):

see therapeutic indication according to marketing authorisation.

1. Additional benefit of the medicinal product in relation to the appropriate comparator therapy

Adults with treatment-resistant Major Depressive Disorder, who have not responded to at least two different treatments with antidepressants in the current moderate to severe depressive episode.

Appropriate comparator therapy:

Therapy according to the doctor's instructions under the selection of:

- augmentation with lithium[1] or quetiapine retard
- a combination with a second antidepressant[1]
- electroconvulsive therapy
- a change from antidepressant monotherapy to another substance class.

Extent and likelihood of additional benefit of esketamine in combination with SSRI or SNRI compared with the appropriate comparator therapy:

An additional benefit is not proven.

1 As an add-on to the last antidepressant monotherapy given.

Study results according to endpoints:

Adults with treatment-resistant Major Depressive Disorder, who have not responded to at least two different treatments with antidepressants in the current moderate to severe depressive episode

There are no assessable data.

Summary of results for relevant clinical endpoints

Endpoint category	Direction of effect/ risk of bias	Summary
Mortality	n.a.	There are no assessable data.
Morbidity	n.a.	There are no assessable data.
Health-related quality of life	∅	There are no data.
Side effects	n.a.	There are no assessable data.

Explanations:
↑: statistically significant and relevant positive effect with low/unclear reliability of data
↓: statistically significant and relevant negative effect with low/unclear reliability of data
↑↑: statistically significant and relevant positive effect with high reliability of data
↓↓: statistically significant and relevant negative effect with high reliability of data
↔: no statistically significant or relevant difference
∅: there are no usable data for the benefit assessment.
n.a.: not assessable

2. Number of patients or demarcation of patient groups eligible for treatment

Adults with treatment-resistant Major Depressive Disorder, who have not responded to at least two different treatments with antidepressants in the current moderate to severe depressive episode

approx. 932,000 – 974,000 patients

3. Requirements for a quality-assured application

The requirements in the product information are to be taken into account. The European Medicines Agency (EMA) provides the contents of the product information (summary of product characteristics, SmPC) for Spravato (active ingredient: esketamine) at the following publicly accessible link (last access: 25 May 2021):

https://www.ema.europa.eu/en/documents/product-information/spravato-epar-product-information_de.pdf

Treatment with Spravato may only be initiated and monitored by a psychiatrist.

The use of Spravato and subsequent follow-up must take place in an appropriate medical setting.

Spravato must not be used if increased blood pressure or increased intracranial pressure poses a serious risk.

Patients with clinically significant or unstable cardiovascular or respiratory disease require additional precautions. For these patients, Spravato must be used in a setting where appropriate resuscitation equipment and healthcare professionals trained in cardiopulmonary resuscitation are available.

In accordance with the European Medicines Agency, the pharmaceutical company must provide training material and a patient guideline. The following training material must be made available to healthcare professionals: Guideline for healthcare professionals with information on specific risks and a checklist for healthcare professionals.

The patient guideline has to be made available to patients.

4. Treatment costs

Annual treatment costs:

Adults with treatment-resistant Major Depressive Disorder, who have not responded to at least two different treatments with antidepressants in the current moderate to severe depressive episode

Designation of the therapy	Annual treatment costs/patient
Medicinal product to be assessed:	
Esketamine[2]	€ 10,715.36 - € 64,168.97
Selective serotonin reuptake Inhibitors (SSRI)	
Citalopram	€ 59.02 - € 147.61
Escitalopram	€ 53.36- € 114.39
Fluoxetine	€ 87.75 - € 221.77
Fluvoxamine	€ 71.18 - € 213.53
Paroxetine	€ 87.75 - € 196.84
Sertraline	€ 103.48 - € 226.92
Serotonin-norepinephrine reuptake inhibitors (SNRIs)	

2 Esketamine is listed in the LAUER-TAXE® as a clinic pack only. Accordingly, the active ingredient is not subject to the Pharmaceutical Price Ordinance (Arzneimittelpreisverordnung) and no rebates according to Section 130 or Section 130a SGB V apply. The calculation is based on the purchase price of the clinic package (information from the pharmaceutical company) plus 19 % value added tax.

Designation of the therapy	Annual treatment costs/patient
Venlafaxine	€ 130.78 - € 427.85
Duloxetine	€ 282.33 – € 564.66
Milnacipran	€ 546.26
Total: Esketamine + SSRI or SNRI:	€ 10,768.72 - € 64,733.63
Appropriate comparator therapy:	
Lithium augmentation	
Lithium	€ 158.99- € 317.99
Antidepressant*	€ 53.36 - € 701.82[3]
Total:	€ 212.35 - € 1,019.81
Augmentation with quetiapine retard	
Quetiapine	€ 169.10 - € 282.18
Antidepressant*	€ 53.36 - € 701.82[3]
Total:	€ 222.46 - € 984.00
Combination with a second antidepressant:	
Antidepressant*	€ 53.36 - € 701.82[3]
Mirtazapine or mianserin	€ 82.56 - € 488.70
Total	€ 135.92 - € 1,190.52
Change of antidepressant monotherapy	
Antidepressant*	€ 53,36 - € 1,575.63[4]
*) Antidepressants	
Tri- and tetracyclic antidepressants (TCA) / non-selective monoamine reuptake inhibitors (NSMRI)	
Amitriptyline oxide	€ 66.65 - € 123.30
Amitriptyline	€ 76.07 - € 190.53
Clomipramine	€ 109.63 - € 438.51
Doxepin	€ 66.80 - € 160.53
Imipramine	€ 106.80 - € 205.68
Maprotiline	€ 56.79 - € 205.13
Nortriptyline	€ 55.66 - € 333.98
Trimipramine	€ 93.73 - € 374.93

3 The range is composed of the lower limit for escitalopram and the upper limit for trazodone. Tranylcypromine should only be used as a reserve antidepressant, according to the product information (Jatrosom, last revised April 2021), and a combination with tricyclic antidepressants is only indicated in individual cases and is therefore not considered here.
4 The range is composed of the lower limit for escitalopram and the upper limit for tranylcypromine.

Designation of the therapy	Annual treatment costs/patient
Selective serotonin reuptake inhibitors (SSRIs)	
Citalopram	€ 59.02 - € 147.61
Escitalopram	€ 53.36- € 114.39
Fluoxetine	€ 87.75 - € 221.77
Fluvoxamine	€ 71.18 - € 213.53
Paroxetine	€ 87.75 - € 196.84
Sertraline	€ 103.48 - € 226.92
Monoamine oxidase inhibitors (MAOIs)	
Moclobemide	€ 186.84 - € 606.56
Tranylcypromine	€ 410.73 - € 1,575.63
Serotonin-norepinephrine reuptake inhibitors (SNRIs)	
Venlafaxine	€ 130.78 - € 427.85
Duloxetine	€ 282.33 - € 564.66
Milnacipran	€ 546.26
Other antidepressants	
Mianserin	€ 175.46 - € 488.70
Mirtazapine	€ 82.56 - € 211.63
Bupropion	€ 328.54 - € 281.86
Agomelatine	€ 238.59 - € 477.18
Tianeptine	€ 333.29 - € 499.94
Trazodone	€ 175.46 - € 701,82
Electroconvulsive therapy	
Acute therapy	€ 6,928.10
Inpatient stay - acute therapy	Incalculable
Maintenance treatment	Patient-individual
Inpatient stay - maintenance treatment	Incalculable

Costs after deduction of statutory rebates (LAUER-TAXE® as last revised: 1 August 2021)

Costs for additionally required SHI services: not applicable

II. Entry into force

1. The resolution will enter into force on the day of its publication on the internet on the website of the Federal Joint Committee on 19 August 2021.

2. The period of validity of the resolution is limited to 15 June 2023.

The justification to this resolution will be published on the website of the G-BA at www.g-ba.de.

Berlin, 19 August 2021

Federal Joint Committee (G-BA)
in accordance with Section 91 SGB V
The Chair

Prof. Hecken